

2-ethylhexyl palmitate or a blend of branched chain esters may be used. These may be used alone or in combination depending on the properties required. Alternatively, high melting point lipids such as white soft paraffin and/or liquid paraffin or other mineral oils can be used.

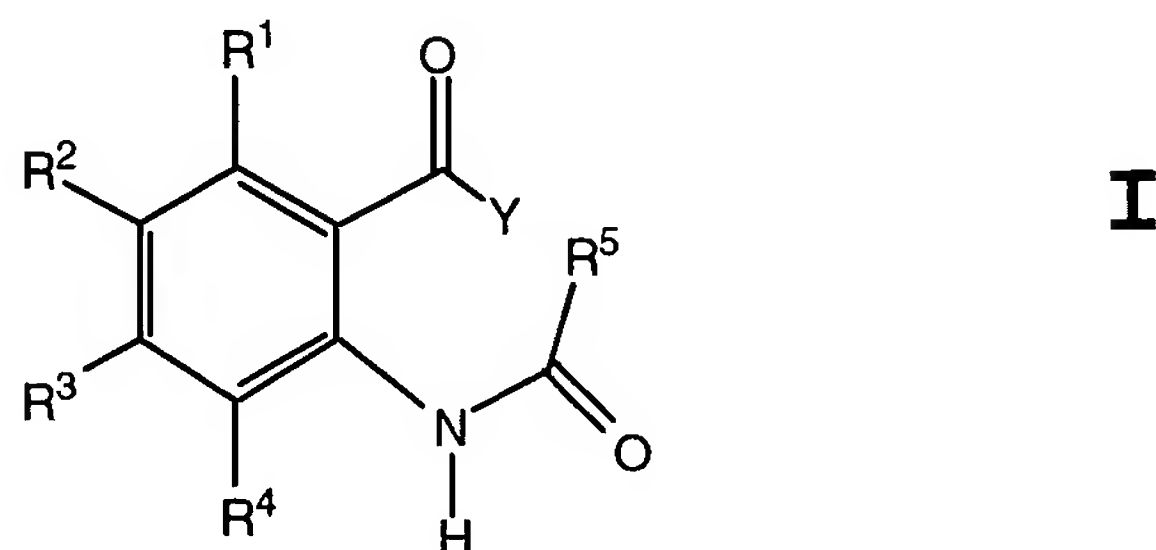
5 Formulations suitable for topical administration to the eye also include eye drops wherein the active ingredients are dissolved or suspended in suitable carrier, especially an aqueous solvent for the active ingredients. The antiviral active ingredients are preferably present in such formulations in a concentration of 0.5 to 20%, advantageously 0.5 to 10% and particularly about 1.5% w/w.

10 Although this invention has been described with respect to specific embodiments, the details of these embodiments are not to be construed as limitations.

What is claimed is:

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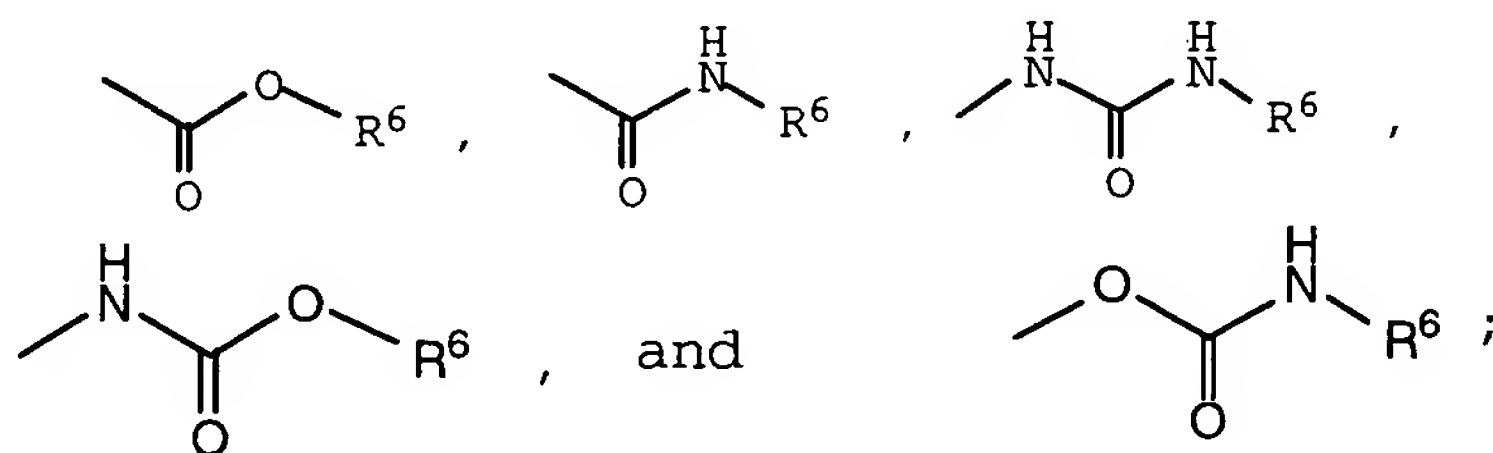
1. A compound of Formula I



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wherein each of R¹, R², R³, and R⁴ is independently selected from hydrido, alkyl, aralkyl, halo, alkoxy, cyano, nitro, amino, alkylamino, N-acylamino, alkylsulfonyloxy, aminosulfonyl, N-(haloalkylcarbonyl)amino, peptidyl, amino acid residue,

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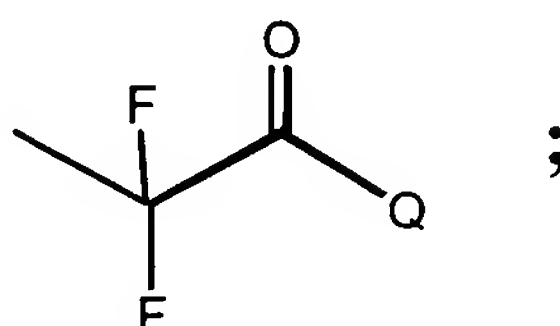
wherein R⁵ is selected from alkoxy, aryloxy, aralkyloxy, alkylthio, arylthio, aralkylthio, alkylamino, arylamino, aralkylamino, alkyl, aryl, aralkyl,

heterocyclyl, and heterocyclylalkyl, wherein R^5 is optionally substituted at a substitutable position with one or more substituents selected from alkyl, alkoxy, aryloxy, alkylthio, arylthio, halo, nitro, N-acylamino, amino, alkylamino, alkoxycarbonyl, amino acid residue and peptidyl;

5 wherein R^6 is selected from alkyl, aryl, aralkyl, heterocyclyl and heterocyclylalkyl, wherein R^6 is optionally substituted at a substitutable position with a radical selected from alkoxy, aryloxy, alkylthio, arylthio, halo, nitro, N-acylamino, amino, alkylamino and alkoxycarbonyl;

wherein Y is selected from fluoroalkyl and

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wherein Q is selected from alkoxy, aryloxy, aralkyloxy, amino acid residue, peptidyl, and $-NHR^7$; and

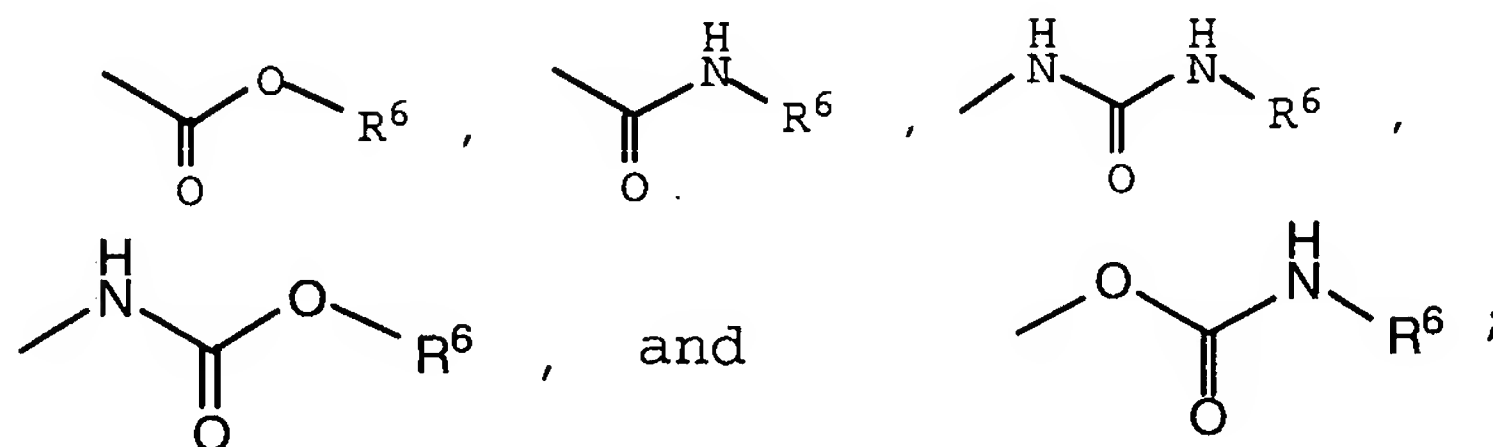
15 wherein R^7 is a radical selected from alkyl, aralkyl, and heterocyclylalkyl, wherein R^7 is optionally substituted at a substitutable position with a radical selected from amino, nitrogen-containing heterocyclyl and alkylamino;

or a pharmaceutically-acceptable salt or tautomer thereof.

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2. Compound of Claim 1 wherein each of R^1 , R^2 , R^3 , and R^4 is independently selected from hydrido, lower alkyl, lower aralkyl, halo, lower alkoxy, cyano, nitro, amino, lower alkylamino, N-acylamino, lower alkylsulfonyloxy, aminosulfonyl, lower N-(haloalkylcarbonyl)amino, amino acid residue, peptidyl,

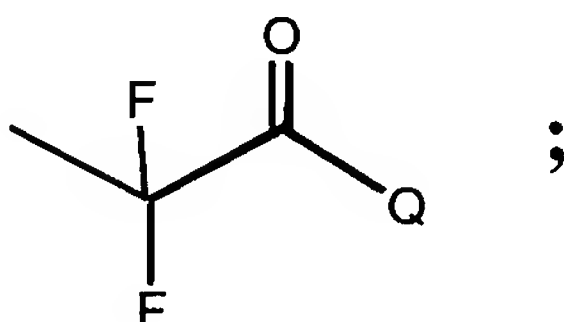
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wherein R^5 is selected from lower alkoxy, phenyloxy, lower aralkyloxy, lower alkylthio, phenylthio, lower aralkylthio, lower alkylamino, arylamino, lower

aralkylamino, lower alkyl, 6-10-membered aryl, lower aralkyl, 5-10-membered heterocyclyl, and lower heterocyclylalkyl, wherein R^5 is optionally substituted at a substitutable position with one or more substituents selected from lower alkyl, lower alkoxy, phenoxy, lower alkylthio, phenylthio, halo, nitro, N-acylamino, amino, lower alkylamino, lower alkoxycarbonyl, amino acid residue and peptidyl; wherein R^6 is selected from lower alkyl, 6-10-membered aryl, lower aralkyl, 5-10-membered heterocyclyl and lower heterocyclylalkyl, wherein R^6 is optionally substituted at a substitutable position with a radical selected from lower alkoxy, phenoxy, lower alkylthio, phenylthio, halo, nitro, N-acylamino, amino, lower alkylamino, and lower alkoxycarbonyl; wherein Y is selected from lower fluoroalkyl and

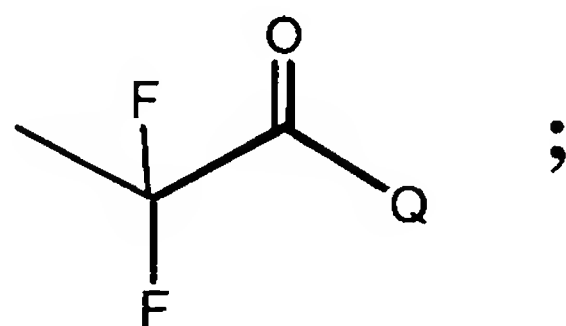


wherein Q is selected from lower alkoxy, phenoxy, lower aralkyloxy, N-amino acid residue, N-peptidyl, and $-NHR^7$; and wherein R^7 is a radical selected from lower alkyl, lower aralkyl, and lower heterocyclylalkyl, wherein R^7 is optionally substituted at a substitutable position with one or more radical selected from amino, 5-6-membered nitrogen-containing heterocyclyl and lower N,N-dialkylamino; or a pharmaceutically-acceptable salt or tautomer thereof.

3. Compound of Claim 2 wherein Y is lower fluoroalkyl; wherein each of R^1 , R^2 , R^3 , and R^4 is independently selected from hydrido, lower alkyl, halo, lower alkoxy, nitro, and amino; and wherein R^5 is selected from phenylalkoxy, lower alkyl substituted with halo or phenoxy, phenyl, lower phenylalkyl, and five-ten membered heteroaryl, wherein R^5 is optionally substituted at a substitutable position of a phenyl or heteroaryl radical with one or more substituents selected from lower alkyl, lower alkoxy, phenoxy, lower alkylthio, phenylthio, halo, nitro, N-acylamino, amino, lower alkylamino, lower alkoxycarbonyl, amino acid residue, and peptidyl; or a pharmaceutically-acceptable salt or tautomer thereof.

4. Compound of Claim 3 wherein Y is selected from difluoromethyl, trifluoromethyl, pentafluoroethyl, heptafluoropropyl, 1,1-difluoroethyl, and 1,1-difluoropropyl; wherein each of R¹, R², R³, and R⁴ is independently selected from hydrido, methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, *tert*-butyl, pentyl, hexyl, fluoro, chloro, bromo, iodo, methoxy, ethoxy, propoxy, isopropoxy, butoxy, *tert*-butoxy, nitro, and amino; wherein R⁵ is selected from phenylmethoxy, phenylethoxy, phenylpropoxy, fluoromethyl, difluoromethyl, trifluoromethyl, chloromethyl, dichloromethyl, trichloromethyl, pentafluoroethyl, heptafluoropropyl, difluorochloromethyl, dichlorofluoromethyl, difluoroethyl, difluoropropyl, dichloroethyl, dichloropropyl, phenyloxyethyl, phenyloxypropyl, phenyl, phenylmethyl, phenylethyl, furyl, pyrazinyl, oxazolyl, thiazolyl, thienyl, pyrrolyl, benzothienyl, benzofuranyl, indolyl, and pyridyl, wherein R⁵ is optionally substituted at a substitutable position of a phenyl or heteroaryl radical with one or more substituents selected from methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, *tert*-butyl, pentyl, hexyl, methoxy, ethoxy, propoxy, isopropoxy, butoxy, *tert*-butoxy, phenyloxy, methylthio, phenylthio, fluoro, chloro, bromo, iodo, nitro, N-formylamino, acetylamino, amino, N,N-dimethylamino and methoxycarbonyl; or a pharmaceutically-acceptable salt or tautomer thereof.

5. Compound of Claim 2 wherein Y is



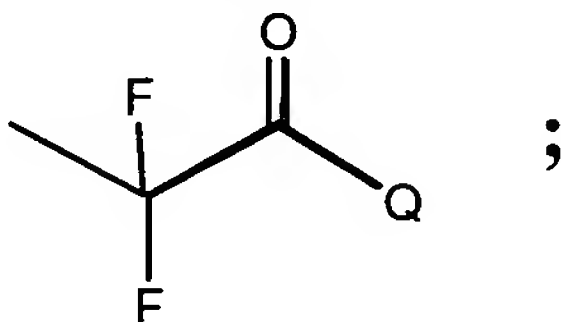
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wherein Q is selected from lower alkoxy, phenyloxy, lower aralkyloxy, N-amino acid residue, N-peptidyl, and -NHR⁷; and wherein R⁷ is a radical selected from lower alkyl, lower aralkyl, and lower heteroaralkyl, wherein R⁷ is optionally substituted at a substitutable position with a radical selected from amino, 5-6 membered nitrogen-containing heterocyclyl and lower N,N-dialkylamino; wherein each of R¹, R², R³, and R⁴ is independently selected from hydrido, lower alkyl, halo, lower alkoxy, nitro, and amino; and wherein R⁵ is selected from phenylalkoxy, lower alkyl

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substituted with halo or phenyloxy, phenyl, lower phenylalkyl, and five-ten
 membered heteroaryl, wherein R^5 is optionally substituted at a
 substitutable position of a phenyl or heteroaryl radical with one or more
 substituents selected from lower alkyl, lower alkoxy, phenyloxy, lower
 5 alkylthio, phenylthio, halo, nitro, N-acylamino, amino, lower alkylamino,
 lower alkoxycarbonyl, amino acid residue, and peptidyl; or a
 pharmaceutically-acceptable salt or tautomer thereof.

6. Compound of Claim 5 wherein Y is

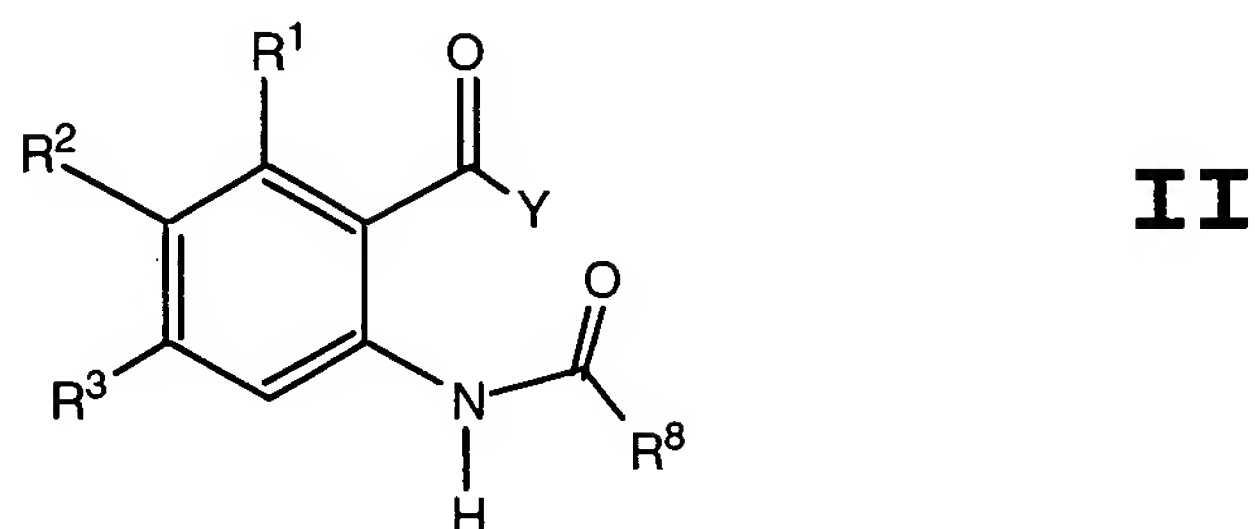


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wherein Q is selected from methoxy, ethoxy, propoxy, isopropoxy, butoxy,
 phenyloxy, benzyloxy, phenylethoxy, and $-NHR^7$; and wherein R^7 is a
 radical selected from methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl,
 15 sec-butyl, *tert*-butyl, pentyl, hexyl, benzyl, phenethyl, oxazolylmethyl,
 oxazolylethyl, imidazolylmethyl, imidazolylethyl, oxazolinylmethyl,
 oxazolinylethyl, indolylethyl, indolylmethyl, pyridylmethyl, thienylmethyl,
 and furylethyl, wherein R^7 is optionally substituted at a substitutable
 position with a radical selected from amino, piperidiny, piperazinyl,
 20 pyrrolidinyl, morpholinyl, pyridyl, pyrimidyl and N,N-dimethylamino;
 wherein each of R^1 , R^2 , R^3 , and R^4 is independently selected from hydrido,
 methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, *tert*-butyl,
 pentyl, hexyl, fluoro, chloro, bromo, iodo, methoxy, ethoxy, propoxy,
 isopropoxy, butoxy, *tert*-butoxy, nitro, and amino; and wherein R^5 is
 25 selected from phenylmethoxy, phenylethoxy, phenylpropoxy, fluoromethyl,
 difluoromethyl, trifluoromethyl, chloromethyl, dichloromethyl,
 pentafluoroethyl, heptafluoropropyl, difluorochloromethyl,
 dichlorofluoromethyl, difluoroethyl, difluoropropyl, dichloroethyl,
 dichloropropyl, phenyloxyethyl, phenyloxypropyl, phenyl, phenylmethyl,
 30 phenylethyl, furyl, pyrazinyl, oxazolyl, thiazolyl, thienyl, pyrrolyl,
 benzothienyl, benzofuranyl, indolyl, and pyridyl, wherein R^5 is optionally
 substituted at a substitutable position on a phenyl or heteroaryl radical with
 one or more substituents selected from methyl, ethyl, n-propyl, isopropyl,
 n-butyl, isobutyl, sec-butyl, *tert*-butyl, pentyl, hexyl, methoxy, ethoxy,

propoxy, isopropoxy, butoxy, *tert*-butoxy, *tert*-butoxy, phenyloxy, methylthio, phenylthio, fluoro, chloro, bromo, iodo, nitro, N-formylamino, N-acetylamino, amino, N,N-dimethylamino and methoxycarbonyl; or a pharmaceutically-acceptable salt or tautomer thereof.

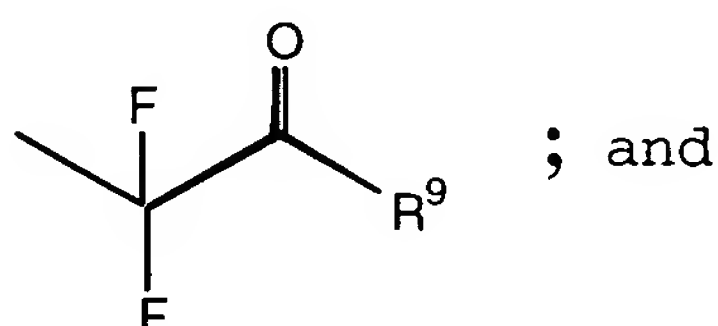
7. A compound of Formula II



5 wherein each of R¹, R², and R³ is independently selected from hydrido, halo, and nitro;

 wherein R⁸ is selected from haloalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, optionally substituted arylalkoxy and optionally substituted aryloxyalkyl;

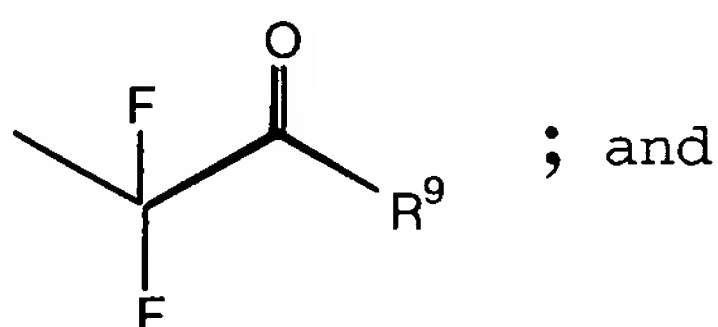
10 wherein Y is selected from fluoroalkyl, and



 wherein R⁹ is alkylamino;

15 or a pharmaceutically-acceptable salt or tautomer thereof.

8. Compound of Claim 7 wherein R¹ is selected from hydrido, fluoro, chloro, bromo and iodo; wherein R² is selected from hydrido, fluoro, chloro, bromo and iodo; wherein R³ is selected from hydrido, fluoro, chloro, bromo, iodo and nitro; wherein R⁸ is selected from trifluoromethyl, phenyl, phenylmethyl, phenylethyl, furyl, pyridyl, pyrazinyl, thienyl, pyrrolyl, benzothienyl, benzofuranyl, indolyl, phenylmethoxy, (phenyloxy)propyl and phenyloxymethyl; wherein Y is selected from trifluoromethyl and

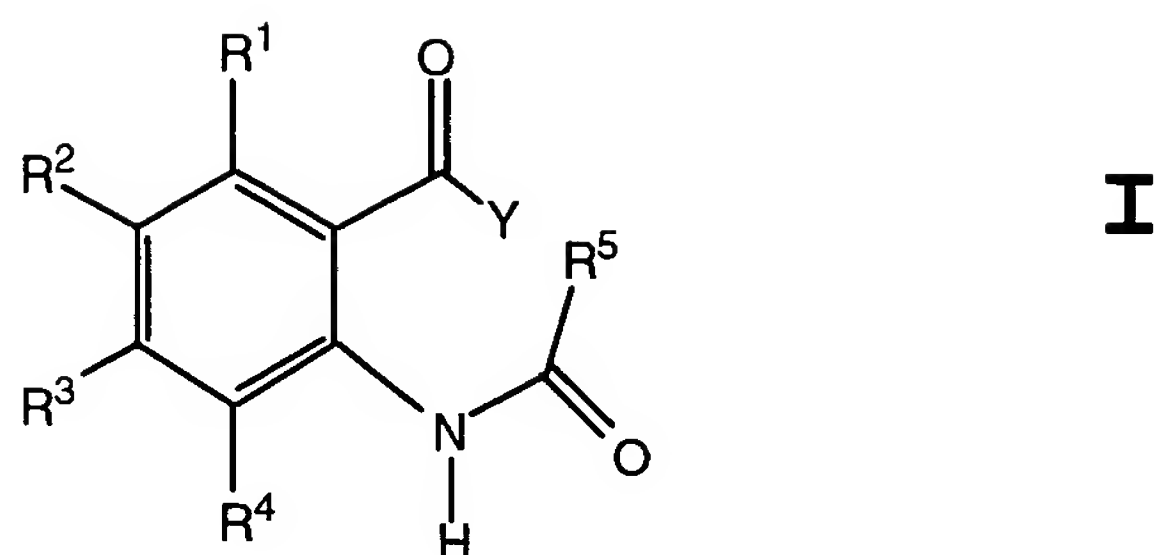


wherein R⁹ is selected from methylamino, ethylamino, propylamino, isopropylamino and N,N-dimethylamino; or a pharmaceutically-acceptable salt or tautomer thereof.

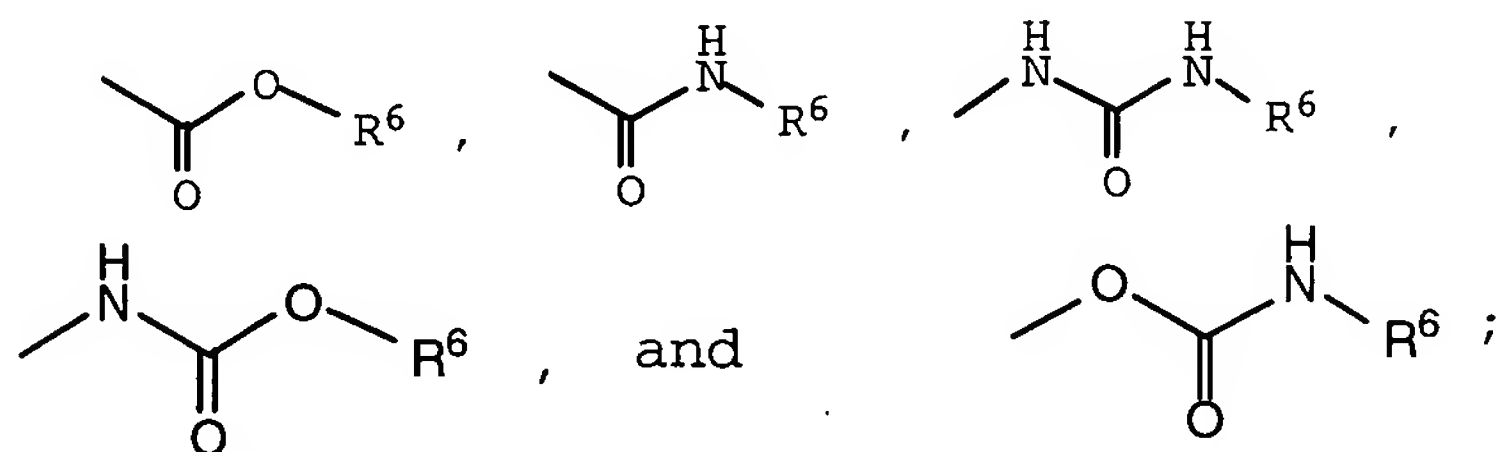
- 5 9. Compound of Claim 8 selected from compounds and their pharmaceutically-acceptable salts, of the group consisting of

10 ?-phenoxy-N-[2-(2,2,2-trifluoro-1-oxo-ethyl)phenyl]butanamide;
 N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]furan-2-carboxamide;
 N-[5-fluoro-2-(2,2,2-trifluoro-1-oxoethyl)phenyl]benzenepropanamide;
 N-[3-chloro-2-(2,2,2-trifluoro-1-oxoethyl)phenyl]benzenepropanamide;
 N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]benzenepropanamide;
 15 N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]pyrazine-2-carboxamide;
 phenylmethyl N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]carbamate;
 N-[5-nitro-2-(2,2,2-trifluoro-1-oxoethyl)phenyl]benzenepropanamide;
 N-[4-fluoro-2-(2,2,2-trifluoro-1-oxoethyl)phenyl]furan-2-
 20 carboxamide;
 N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]-1-benzothiophene-2-
 carboxamide;
 ?,?,?-trifluoro-N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]acetamide;
 N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]pyridine-2-carboxamide;
 25 N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]2-methoxybenzamide;
 N-[4-iodo-2-(2,2,2-trifluoro-1-oxoethyl)phenyl]furan-2-
 carboxamide;
 N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]4-chlorophenoxyacetamide;
 N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]indolyl-2-carboxamide;
 30 N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]benzofuranyl-2-
 carboxamide; and
 N-[2-(3-(2-propylamino)-3-oxo-2,2-difluoro-1-oxopropyl)phenyl]2-
 methoxyphenylcarboxamide.

- 35 10. A pharmaceutical composition comprising a therapeutically-effective amount of a compound and a pharmaceutically-acceptable carrier or diluent, said compound selected from a compound of Formula I



wherein each of R¹, R², R³, and R⁴ is independently selected from
 5 hydrido, alkyl, aralkyl, halo, alkoxy, cyano, nitro, amino, alkylamino, N-
 acylamino, alkylsulfonyloxy, aminosulfonyl, N-(haloalkylcarbonyl)amino,
 peptidyl, amino acid residue,

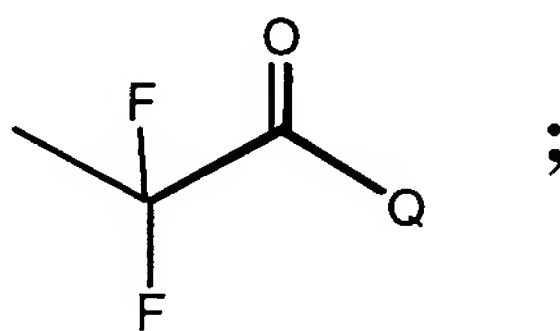


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wherein R⁵ is selected from alkoxy, aryloxy, aralkyloxy, alkylthio,
 arylthio, aralkylthio, alkylamino, arylamino, aralkylamino, alkyl, aryl, aralkyl,
 heterocyclyl, and heterocyclylalkyl, wherein R⁵ is optionally substituted at a
 15 substitutable position with one or more substituents selected from alkyl, alkoxy,
 aryloxy, alkylthio, arylthio, halo, nitro, N-acylamino, amino, alkylamino,
 alkoxycarbonyl, amino acid residue and peptidyl;

wherein R⁶ is selected from alkyl, aryl, aralkyl, heterocyclyl and
 heterocyclylalkyl, wherein R⁶ is optionally substituted at a substitutable position
 20 with a radical selected from alkoxy, aryloxy, alkylthio, arylthio, halo, nitro, N-
 acylamino, amino, alkylamino and alkoxycarbonyl;

wherein Y is selected from fluoroalkyl and

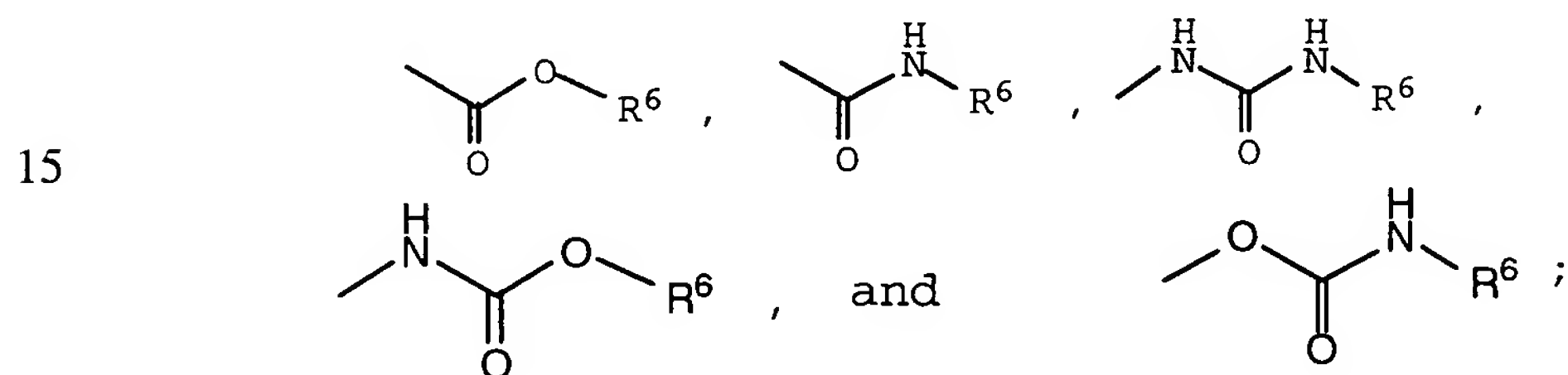


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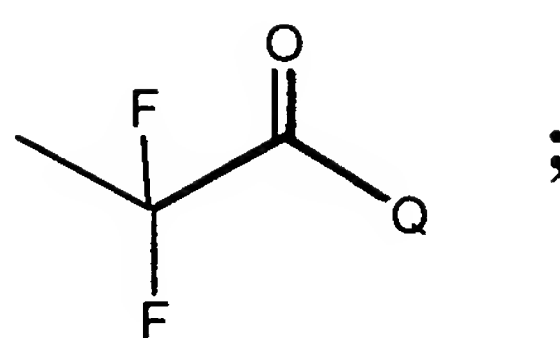
wherein Q is selected from alkoxy, aryloxy, aralkyloxy, amino acid residue, peptidyl, and -NHR^7 ; and

wherein R^7 is a radical selected from alkyl, aralkyl, and heterocyclalkyl, wherein R^7 is optionally substituted at a substitutable position with a radical selected from amino, nitrogen-containing heterocycl and alkylamino;
or a pharmaceutically-acceptable salt or tautomer thereof.

11. A pharmaceutical composition of Claim 10 wherein each of R^1 , R^2 , R^3 , and R^4 is independently selected from hydrido, lower alkyl, lower aralkyl, halo, lower alkoxy, cyano, nitro, amino, lower alkylamino, N-acylamino, lower alkylsulfonyloxy, aminosulfonyl, lower N-(haloalkylcarbonyl)amino, amino acid residue, peptidyl,



wherein R^5 is selected from lower alkoxy, phenyloxy, lower aralkyloxy, lower alkylthio, phenylthio, lower aralkylthio, lower alkylamino, arylamino, lower aralkylamino, lower alkyl, 6-10-membered aryl, lower aralkyl, 5-10-membered heterocycl, and lower heterocyclalkyl, wherein R^5 is optionally substituted at a substitutable position with one or more substituents selected from lower alkyl, lower alkoxy, phenyloxy, lower alkylthio, phenylthio, halo, nitro, N-acylamino, amino, lower alkylamino, lower alkoxycarbonyl, amino acid residue and peptidyl; wherein R^6 is selected from lower alkyl, 6-10-membered aryl, lower aralkyl, 5-10-membered heterocycl and lower heterocyclalkyl, wherein R^6 is optionally substituted at a substitutable position with a radical selected from lower alkoxy, phenyloxy, lower alkylthio, phenylthio, halo, nitro, N-acylamino, amino, lower alkylamino, and lower alkoxycarbonyl; wherein Y is selected from lower fluoroalkyl and



wherein Q is selected from lower alkoxy, phenoxy, lower aralkoxy, N-amino acid residue, N-peptidyl, and -NHR⁷; and wherein R⁷ is a radical selected from lower alkyl, lower aralkyl, and lower heterocyclalkyl, wherein R⁷ is optionally substituted at a substitutable position with one or more radical selected from amino, 5-6-membered nitrogen-containing heterocycl and lower N,N-dialkylamino; or a pharmaceutically-acceptable salt or tautomer thereof.

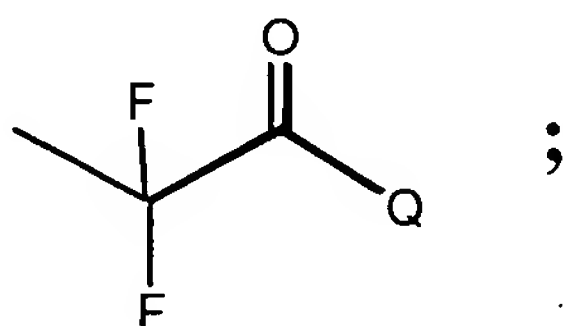
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12. A pharmaceutical composition of Claim 11 wherein Y is lower fluoroalkyl; wherein each of R¹, R², R³, and R⁴ is independently selected from hydrido, lower alkyl, halo, lower alkoxy, nitro, and amino; and wherein R⁵ is selected from phenylalkoxy, lower alkyl substituted with halo or phenoxy, phenyl, lower phenylalkyl, and five-ten membered heteroaryl, wherein R⁵ is optionally substituted at a substitutable position of a phenyl or heteroaryl radical with one or more substituents selected from lower alkyl, lower alkoxy, phenoxy, lower alkylthio, phenylthio, halo, nitro, N-acylamino, amino, lower alkylamino, lower alkoxycarbonyl, amino acid residue, and peptidyl; or a pharmaceutically-acceptable salt or tautomer thereof.

13. A pharmaceutical composition of Claim 12 wherein Y is selected from difluoromethyl, trifluoromethyl, pentafluoroethyl, heptafluoropropyl, 1,1-difluoroethyl, and 1,1-difluoropropyl; wherein each of R¹, R², R³, and R⁴ is independently selected from hydrido, methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, *tert*-butyl, pentyl, hexyl, fluoro, chloro, bromo, iodo, methoxy, ethoxy, propoxy, isopropoxy, butoxy, *tert*-butoxy, nitro, and amino; wherein R⁵ is selected from phenylmethoxy, phenylethoxy, phenylpropoxy, fluoromethyl, difluoromethyl, trifluoromethyl, chloromethyl, dichloromethyl, trichloromethyl, pentafluoroethyl, heptafluoropropyl, difluorochloromethyl, dichlorofluoromethyl, difluoroethyl, difluoropropyl, dichloroethyl, dichloropropyl, phenoxyethyl, phenoxypropyl, phenyl, phenylmethyl,

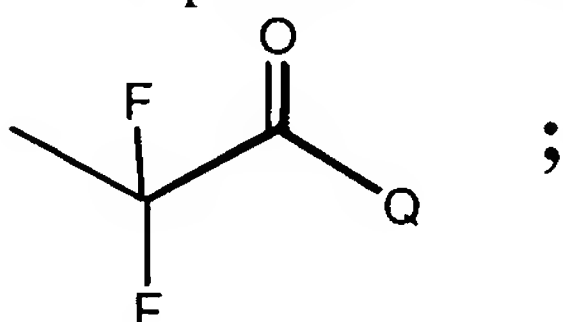
phenylethyl, furyl, pyrazinyl, oxazolyl, thiazolyl, thienyl, pyrrolyl, benzothienyl, benzofuranyl, indolyl, and pyridyl, wherein R^5 is optionally substituted at a substitutable position of a phenyl or heteroaryl radical with one or more substituents selected from methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, *tert*-butyl, pentyl, hexyl, methoxy, ethoxy, propoxy, isopropoxy, butoxy, *tert*-butoxy, phenyloxy, methylthio, phenylthio, fluoro, chloro, bromo, iodo, nitro, N-formylamino, acetylamino, amino, N,N-dimethylamino and methoxycarbonyl; or a pharmaceutically-acceptable salt or tautomer thereof.

14. A pharmaceutical composition of Claim 11 wherein Y is



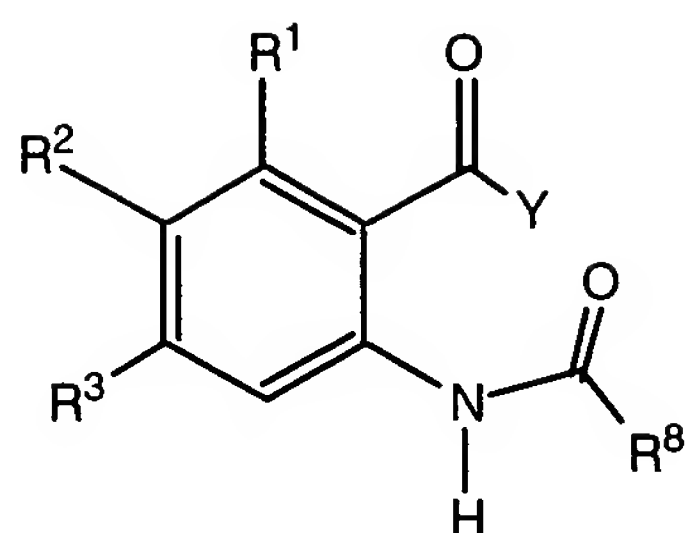
wherein Q is selected from lower alkoxy, phenyloxy, lower aralkyloxy, N-amino acid residue, N-peptidyl, and $-NHR^7$; and wherein R^7 is a radical selected from lower alkyl, lower aralkyl, and lower heteroaralkyl, wherein R^7 is optionally substituted at a substitutable position with a radical selected from amino, 5-6 membered nitrogen-containing heterocyclyl and lower N,N-dialkylamino; wherein each of R^1 , R^2 , R^3 , and R^4 is independently selected from hydrido, lower alkyl, halo, lower alkoxy, nitro, and amino; and wherein R^5 is selected from phenylalkoxy, lower alkyl substituted with halo or phenyloxy, phenyl, lower phenylalkyl, and five-ten membered heteroaryl, wherein R^5 is optionally substituted at a substitutable position of a phenyl or heteroaryl radical with one or more substituents selected from lower alkyl, lower alkoxy, phenyloxy, lower alkylthio, phenylthio, halo, nitro, N-acylamino, amino, lower alkylamino, lower alkoxy carbonyl, amino acid residue, and peptidyl; or a pharmaceutically-acceptable salt or tautomer thereof.

15. A pharmaceutical composition of Claim 14 wherein Y is



wherein Q is selected from methoxy, ethoxy, propoxy, isopropoxy, butoxy, phenyloxy, benzyloxy, phenylethoxy, and -NHR⁷; and wherein R⁷ is a radical selected from methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, *tert*-butyl, pentyl, hexyl, benzyl, phenethyl, oxazolymethyl, oxazolylethyl, imidazolymethyl, imidazolylethyl, oxazolinymethyl, oxazolinylethyl, indolylethyl, indolymethyl, pyridylmethyl, thienylmethyl, and furylethyl, wherein R⁷ is optionally substituted at a substitutable position with a radical selected from amino, piperidinyl, piperazinyl, pyrrolidinyl, morpholinyl, pyridyl, pyrimidyl and N,N-dimethylamino; wherein each of R¹, R², R³, and R⁴ is independently selected from hydrido, methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, *tert*-butyl, pentyl, hexyl, fluoro, chloro, bromo, iodo, methoxy, ethoxy, propoxy, isopropoxy, butoxy, *tert*-butoxy, nitro, and amino; and wherein R⁵ is selected from phenylmethoxy, phenylethoxy, phenylpropoxy, fluoromethyl, difluoromethyl, trifluoromethyl, chloromethyl, dichloromethyl, pentafluoroethyl, heptafluoropropyl, difluorochloromethyl, dichlorofluoromethyl, difluoroethyl, difluoropropyl, dichloroethyl, dichloropropyl, phenyloxyethyl, phenyloxypropyl, phenyl, phenylmethyl, phenylethyl, furyl, pyrazinyl, oxazolyl, thiazolyl, thienyl, pyrrolyl, benzothienyl, benzofuranyl, indolyl, and pyridyl, wherein R⁵ is optionally substituted at a substitutable position on a phenyl or heteroaryl radical with one or more substituents selected from methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, *tert*-butyl, pentyl, hexyl, methoxy, ethoxy, propoxy, isopropoxy, butoxy, *tert*-butoxy, *tert*-butoxy, phenyloxy, methylthio, phenylthio, fluoro, chloro, bromo, iodo, nitro, N-formylamino, N-acetylamino, amino, N,N-dimethylamino and methoxycarbonyl; or a pharmaceutically-acceptable salt or tautomer thereof.

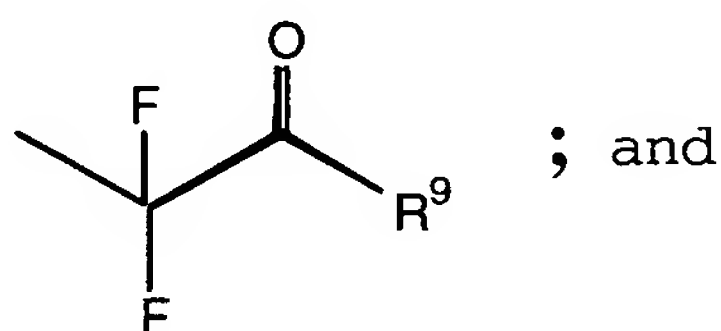
16. A pharmaceutical composition comprising a therapeutically-effective amount of a compound and a pharmaceutically-acceptable carrier or diluent, said compound selected from a compound of Formula II

**II**

wherein each of R^1 , R^2 , and R^3 is independently selected from hydrido, halo, and nitro;

5 wherein R^8 is selected from haloalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, optionally substituted arylalkoxy and optionally substituted aryloxyalkyl;

wherein Y is selected from fluoroalkyl, and



; and

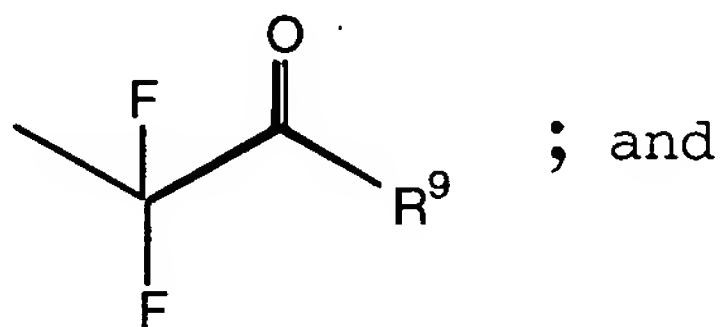
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wherein R^9 is alkylamino;

or a pharmaceutically-acceptable salt or tautomer thereof.

15 17. A pharmaceutical composition of Claim 16 wherein R^1 is selected from hydrido, fluoro, chloro, bromo and iodo; wherein R^2 is selected from hydrido, fluoro, chloro, bromo and iodo; wherein R^3 is selected from hydrido, fluoro, chloro, bromo, iodo and nitro; wherein R^8 is selected from trifluoromethyl, phenyl, phenylmethyl, phenylethyl, furyl, pyridyl, pyrazinyl, thienyl, pyrrolyl, benzothienyl, benzofuranyl, indolyl, phenylmethoxy, (phenoxy)propyl and phenyloxymethyl; wherein Y is selected from trifluoromethyl and

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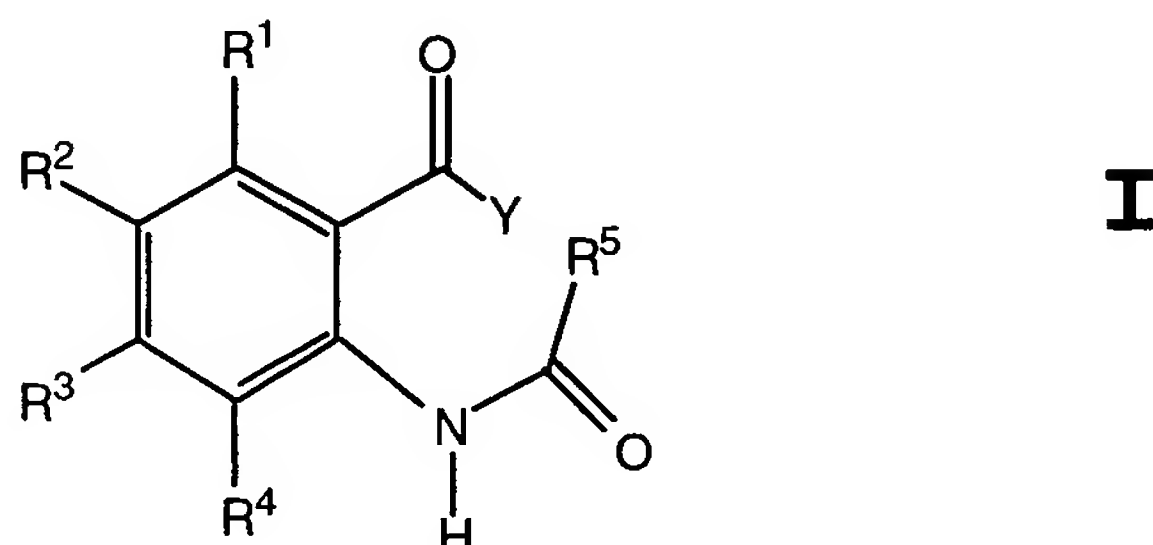
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wherein R⁹ is selected from methylamino, ethylamino, propylamino, isopropylamino and N,N-dimethylamino; or a pharmaceutically-acceptable salt or tautomer thereof.

- 5 18. A pharmaceutical composition of Claim 17 wherein the compound is selected from compounds and their pharmaceutically-acceptable salts, of the group consisting of

- 10 ?-phenoxy-N-[2-(2,2,2-trifluoro-1-oxo-ethyl)phenyl]butanamide;
N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]furan-2-carboxamide;
N-[5-fluoro-2-(2,2,2-trifluoro-1-oxoethyl)phenyl]benzenepropanamide;
N-[3-chloro-2-(2,2,2-trifluoro-1-oxoethyl)phenyl]benzenepropanamide;
15 N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]benzenepropanamide;
N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]pyrazine-2-carboxamide;
phenylmethyl N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]carbamate;
N-[5-nitro-2-(2,2,2-trifluoro-1-oxoethyl)phenyl]benzenepropanamide;
20 N-[4-fluoro-2-(2,2,2-trifluoro-1-oxoethyl)phenyl]furan-2-carboxamide;
N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]-1-benzothiophene-2-carboxamide;
?,?,?-trifluoro-N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]acetamide;
25 N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]pyridine-2-carboxamide;
N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]2-methoxybenzamide;
N-[4-iodo-2-(2,2,2-trifluoro-1-oxoethyl)phenyl]furan-2-carboxamide;
N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]4-chlorophenoxyacetamide;
30 N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]indolyl-2-carboxamide;
N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]benzofuranyl-2-carboxamide; and
N-[2-(3-(2-propylamino)-3-oxo-2,2-difluoro-1-oxopropyl)phenyl]2-methoxyphenylcarboxamide.

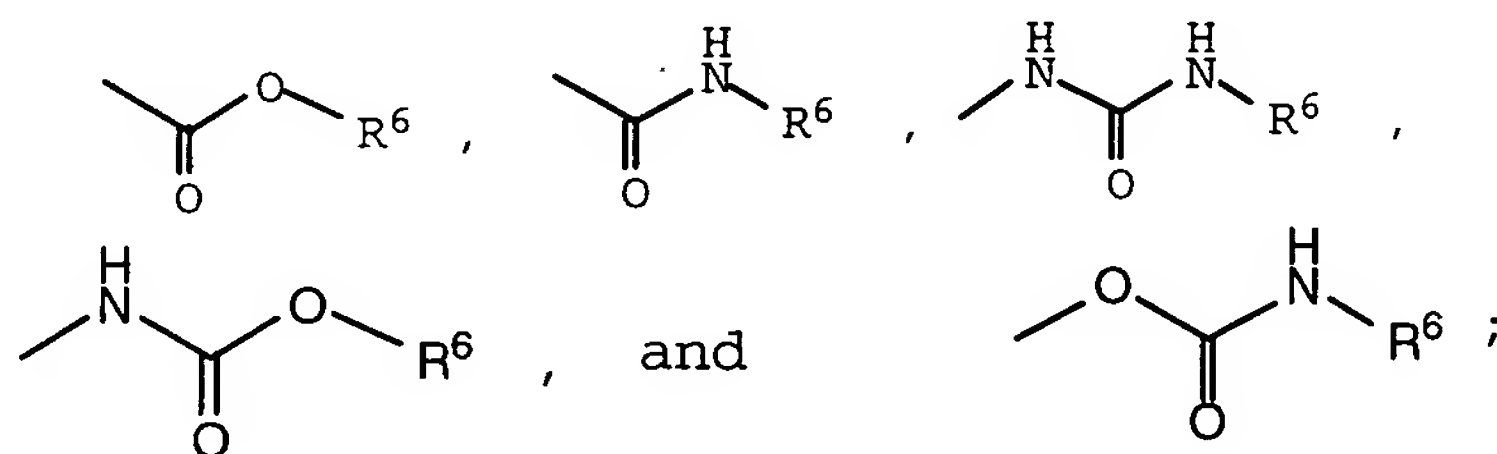
19. A method of treating herpes viral infection in a subject, said method comprising treating said subject with an effective amount of a compound of Formula I



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wherein each of R¹, R², R³, and R⁴ is independently selected from hydrido, alkyl, aralkyl, halo, alkoxy, cyano, nitro, amino, alkylamino, N-acylamino, alkylsulfonyloxy, aminosulfonyl, N-(haloalkylcarbonyl)amino, peptidyl, amino acid residue,

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wherein R⁵ is selected from alkoxy, aryloxy, aralkyloxy, alkylthio, arylthio, aralkylthio, alkylamino, arylamino, aralkylamino, alkyl, aryl, aralkyl, heterocyclyl, and heterocyclylalkyl, wherein R⁵ is optionally substituted at a substitutable position with one or more substituents selected from alkyl, alkoxy, aryloxy, alkylthio, arylthio, halo, nitro, N-acylamino, amino, alkylamino, alkoxycarbonyl, amino acid residue and peptidyl;

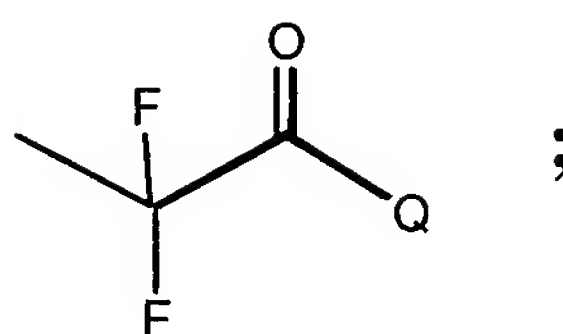
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wherein R⁶ is selected from alkyl, aryl, aralkyl, heterocyclyl and heterocyclylalkyl, wherein R⁶ is optionally substituted at a substitutable position with a radical selected from alkoxy, aryloxy, alkylthio, arylthio, halo, nitro, N-acylamino, amino, alkylamino and alkoxycarbonyl;

25

wherein Y is selected from fluoroalkyl and

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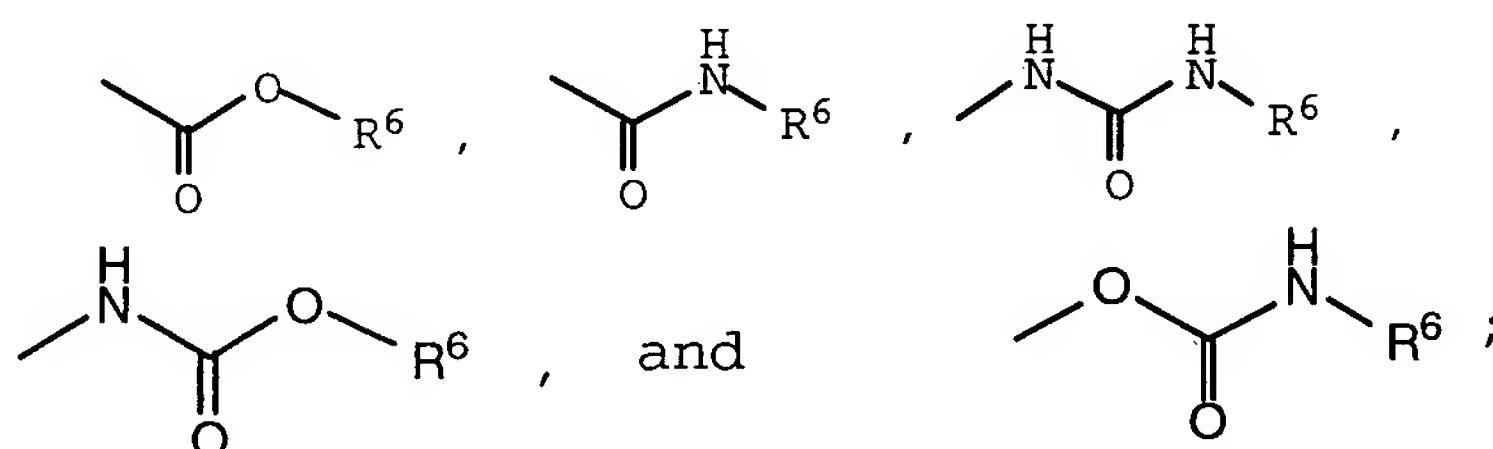
wherein Q is selected from alkoxy, aryloxy, aralkyloxy, amino acid residue, peptidyl, and -NHR^7 ; and

- 5 wherein R^7 is a radical selected from alkyl, aralkyl, and heterocyclalkyl, wherein R^7 is optionally substituted at a substitutable position with a radical selected from amino, nitrogen-containing heterocycl and alkylamino;
or a pharmaceutically-acceptable salt or tautomer thereof.

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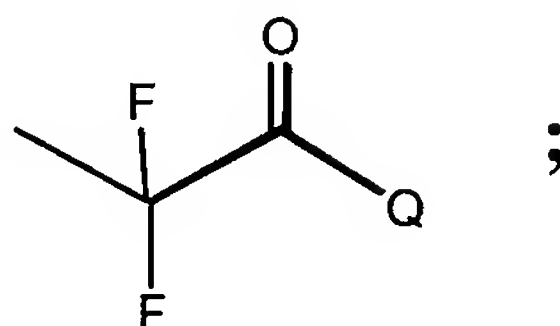
20. A method of Claim 19 wherein each of R^1 , R^2 , R^3 , and R^4 is independently selected from hydrido, lower alkyl, lower aralkyl, halo, lower alkoxy, cyano, nitro, amino, lower alkylamino, N-acylamino, lower alkylsulfonyloxy, aminosulfonyl, lower N-(haloalkylcarbonyl)amino, amino acid residue, peptidyl,

15



- 20 wherein R^5 is selected from lower alkoxy, phenyloxy, lower aralkyloxy, lower alkylthio, phenylthio, lower aralkylthio, lower alkylamino, arylamino, lower aralkylamino, lower alkyl, 6-10-membered aryl, lower aralkyl, 5-10-membered heterocycl, and lower heterocyclalkyl, wherein R^5 is optionally substituted at a substitutable position with one or more substituents selected from lower
25 alkyl, lower alkoxy, phenyloxy, lower alkylthio, phenylthio, halo, nitro, N-acylamino, amino, lower alkylamino, lower alkoxycarbonyl, amino acid residue and peptidyl; wherein R^6 is selected from lower alkyl, 6-10-membered aryl, lower aralkyl, 5-10-membered heterocycl and lower heterocyclalkyl, wherein R^6 is optionally substituted at a substitutable position with a radical
30 selected from lower alkoxy, phenyloxy, lower alkylthio, phenylthio, halo, nitro,

N-acylamino, amino, lower alkylamino, and lower alkoxycarbonyl; wherein Y is selected from lower fluoroalkyl and



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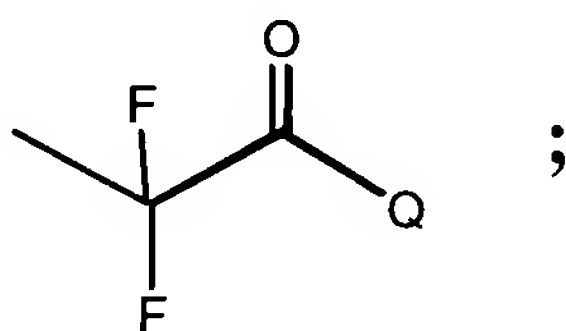
wherein Q is selected from lower alkoxy, phenyloxy, lower aralkyloxy, N-amino acid residue, N-peptidyl, and -NHR⁷; and wherein R⁷ is a radical selected from lower alkyl, lower aralkyl, and lower heterocyclalkyl, wherein R⁷ is optionally substituted at a substitutable position with one or
 10 more radical selected from amino, 5-6-membered nitrogen-containing heterocycl and lower N,N-dialkylamino; or a pharmaceutically-acceptable salt or tautomer thereof.

– 21. A method of Claim 20 wherein Y is lower fluoroalkyl; wherein
 15 each of R¹, R², R³, and R⁴ is independently selected from hydrido, lower alkyl, halo, lower alkoxy, nitro, and amino; and wherein R⁵ is selected from phenylalkoxy, lower alkyl substituted with halo or phenyloxy, phenyl, lower phenylalkyl, and five-ten membered heteroaryl, wherein R⁵ is
 20 optionally substituted at a substitutable position of a phenyl or heteroaryl radical with one or more substituents selected from lower alkyl, lower alkoxy, phenyloxy, lower alkylthio, phenylthio, halo, nitro, N-acylamino, amino, lower alkylamino, lower alkoxycarbonyl, amino acid residue, and peptidyl; or a pharmaceutically-acceptable salt or tautomer thereof.

25 22. A method of Claim 21 wherein Y is selected from difluoromethyl, trifluoromethyl, pentafluoroethyl, heptafluoropropyl, 1,1-difluoroethyl, and 1,1-difluoropropyl; wherein each of R¹, R², R³, and R⁴ is independently selected from hydrido, methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, *tert*-butyl, pentyl, hexyl, fluoro, chloro, bromo,
 30 iodo, methoxy, ethoxy, propoxy, isopropoxy, butoxy, *tert*-butoxy, nitro, and amino; wherein R⁵ is selected from phenylmethoxy, phenylethoxy, phenylpropoxy, fluoromethyl, difluoromethyl, trifluoromethyl, chloromethyl, dichloromethyl, trichloromethyl, pentafluoroethyl, heptafluoropropyl, difluorochloromethyl, dichlorofluoromethyl,

difluoroethyl, difluoropropyl, dichloroethyl, dichloropropyl,
 phenoxyethyl, phenoxypropyl, phenyl, phenylmethyl, phenylethyl,
 furyl, pyrazinyl, oxazolyl, thiazolyl, thienyl, pyrrolyl, benzothienyl,
 benzofuranyl, indolyl, and pyridyl, wherein R⁵ is optionally substituted at a
 5 substitutable position of a phenyl or heteroaryl radical with one or more
 substituents selected from methyl, ethyl, n-propyl, isopropyl, n-butyl,
 isobutyl, sec-butyl, *tert*-butyl, pentyl, hexyl, methoxy, ethoxy, propoxy,
 isopropoxy, butoxy, *tert*-butoxy, phenoxy, methylthio, phenylthio, fluoro,
 chloro, bromo, iodo, nitro, N-formylamino, acetylamino, amino, N,N-
 10 dimethylamino and methoxycarbonyl; or a pharmaceutically-acceptable
 salt or tautomer thereof.

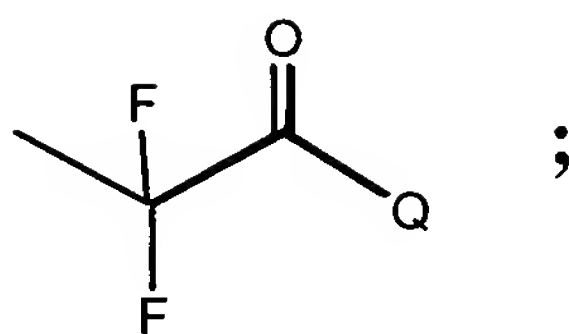
23. A method of Claim 20 wherein Y is



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wherein Q is selected from lower alkoxy, phenoxy, lower aralkyloxy, N-
 amino acid residue, N-peptidyl, and -NHR⁷; and wherein R⁷ is a radical
 selected from lower alkyl, lower aralkyl, and lower heteroaralkyl, wherein
 20 R⁷ is optionally substituted at a substitutable position with a radical
 selected from amino, 5-6 membered nitrogen-containing heterocyclyl and
 lower N,N-dialkylamino; wherein each of R¹, R², R³, and R⁴ is
 independently selected from hydrido, lower alkyl, halo, lower alkoxy, nitro,
 and amino; and wherein R⁵ is selected from phenylalkoxy, lower alkyl
 25 substituted with halo or phenoxy, phenyl, lower phenylalkyl, and five-ten
 membered heteroaryl, wherein R⁵ is optionally substituted at a
 substitutable position of a phenyl or heteroaryl radical with one or more
 substituents selected from lower alkyl, lower alkoxy, phenoxy, lower
 alkylthio, phenylthio, halo, nitro, N-acylamino, amino, lower alkylamino,
 30 lower alkoxycarbonyl, amino acid residue, and peptidyl; or a
 pharmaceutically-acceptable salt or tautomer thereof.

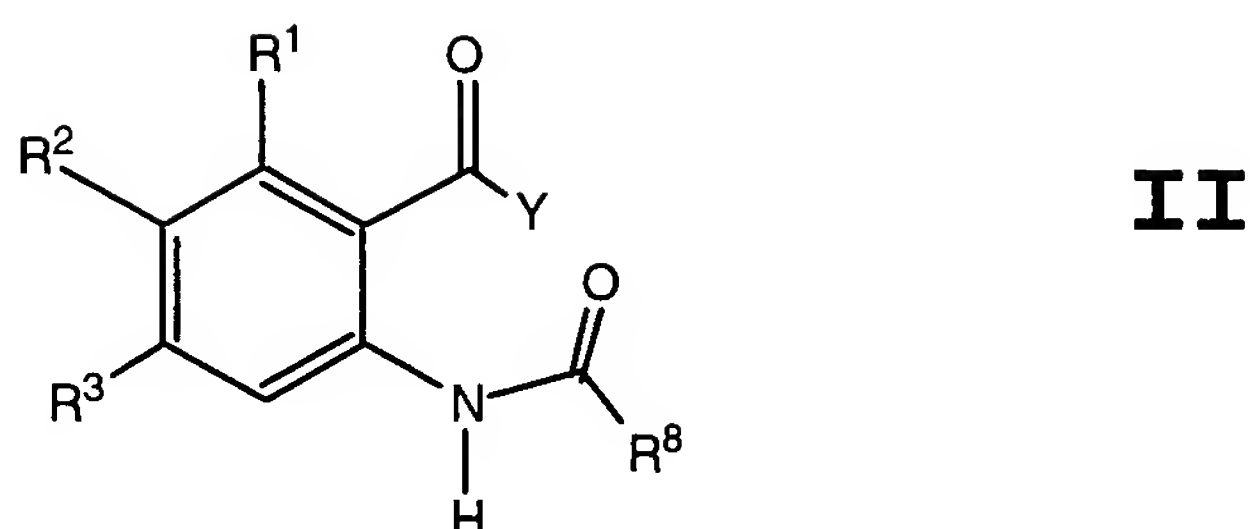
24. A method of Claim 23 wherein Y is



wherein Q is selected from methoxy, ethoxy, propoxy, isopropoxy, butoxy, phenyloxy, benzyloxy, phenylethoxy, and -NHR⁷; and wherein R⁷ is a radical selected from methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, *tert*-butyl, pentyl, hexyl, benzyl, phenethyl, oxazolymethyl, oxazolylethyl, imidazolymethyl, imidazolylethyl, oxazolinymethyl, oxazolinylethyl, indolylethyl, indolymethyl, pyridylmethyl, thienylmethyl, and furylethyl, wherein R⁷ is optionally substituted at a substitutable position with a radical selected from amino, piperidiny, piperazinyl, pyrrolidiny, morpholinyl, pyridyl, pyrimidyl and N,N-dimethylamino; wherein each of R¹, R², R³, and R⁴ is independently selected from hydrido, methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, *tert*-butyl, pentyl, hexyl, fluoro, chloro, bromo, iodo, methoxy, ethoxy, propoxy, isopropoxy, butoxy, *tert*-butoxy, nitro, and amino; and wherein R⁵ is selected from phenylmethoxy, phenylethoxy, phenylpropoxy, fluoromethyl, difluoromethyl, trifluoromethyl, chloromethyl, dichloromethyl, pentafluoroethyl, heptafluoropropyl, difluorochloromethyl, dichlorofluoromethyl, difluoroethyl, difluoropropyl, dichloroethyl, dichloropropyl, phenyloxyethyl, phenyloxypropyl, phenyl, phenylmethyl, phenylethyl, furyl, pyrazinyl, oxazolyl, thiazolyl, thienyl, pyrrolyl, benzothienyl, benzofuranyl, indolyl, and pyridyl, wherein R⁵ is optionally substituted at a substitutable position on a phenyl or heteroaryl radical with one or more substituents selected from methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, *tert*-butyl, pentyl, hexyl, methoxy, ethoxy, propoxy, isopropoxy, butoxy, *tert*-butoxy, *tert*-butoxy, phenyloxy, methylthio, phenylthio, fluoro, chloro, bromo, iodo, nitro, N-formylamino, N-acetylamino, amino, N,N-dimethylamino and methoxycarbonyl; or a pharmaceutically-acceptable salt or tautomer thereof.

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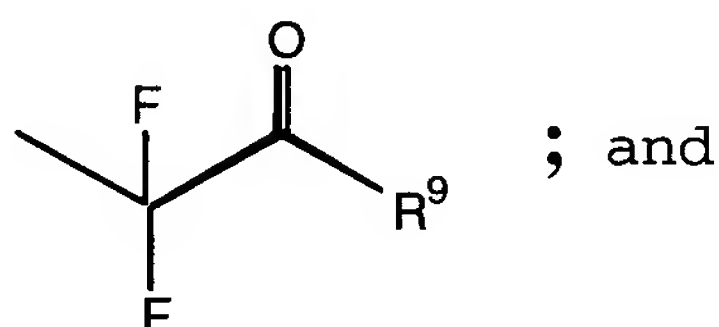
25. A method of treating herpes viral infection in a subject, said method comprising treating said subject with an effective amount of a compound of Formula II



wherein each of R^1 , R^2 , and R^3 is independently selected from hydrido, halo, and nitro;

5 wherein R^8 is selected from haloalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, optionally substituted arylalkoxy and optionally substituted aryloxyalkyl;

wherein Y is selected from fluoroalkyl, and



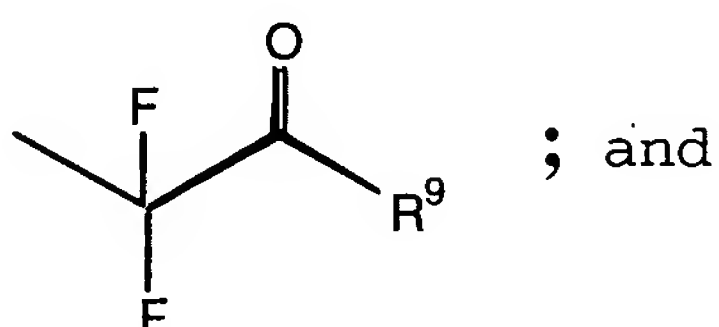
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wherein R^9 is alkylamino;

or a pharmaceutically-acceptable salt or tautomer thereof.

15 26. A method of Claim 25 wherein R^1 is selected from hydrido, fluoro, chloro, bromo and iodo; wherein R^2 is selected from hydrido, fluoro, chloro, bromo and iodo; wherein R^3 is selected from hydrido, fluoro, chloro, bromo, iodo and nitro; wherein R^8 is selected from trifluoromethyl, phenyl, phenylmethyl, phenylethyl, furyl, pyridyl, pyrazinyl, thienyl, pyrrolyl, benzothienyl, benzofuranyl, indolyl, phenylmethoxy, (phenyloxy)propyl and phenyloxymethyl; wherein Y is selected from trifluoromethyl and

20



25 wherein R^9 is selected from methylamino, ethylamino, propylamino, isopropylamino and N,N-dimethylamino; or a pharmaceutically-acceptable salt or tautomer thereof.

27. A method of Claim 26 wherein the compound is selected from compounds and their pharmaceutically-acceptable salts, of the group consisting of

- 5
?-phenoxy-N-[2-(2,2,2-trifluoro-1-oxo-ethyl)phenyl]butanamide;
N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]furan-2-carboxamide;
N-[5-fluoro-2-(2,2,2-trifluoro-1-oxoethyl)phenyl]benzenepropanamide;
10 N-[3-chloro-2-(2,2,2-trifluoro-1-oxoethyl)phenyl]benzenepropanamide;
N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]benzenepropanamide;
N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]pyrazine-2-carboxamide;
phenylmethyl N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]carbamate;
15 N-[5-nitro-2-[2,2,2-trifluoro-1-oxoethyl)phenyl]benzenepropanamide;
N-[4-fluoro-2-(2,2,2-trifluoro-1-oxoethyl)phenyl]furan-2-carboxamide;
N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]-1-benzothiophene-2-carboxamide;
20 ?,?,?-trifluoro-N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]acetamide;
N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]pyridine-2-carboxamide;
N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]2-methoxybenzamide;
N-[4-iodo-2-(2,2,2-trifluoro-1-oxoethyl)phenyl]furan-2-carboxamide;
25 N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]4-chlorophenoxyacetamide;
N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]indolyl-2-carboxamide;
N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]benzofuranyl-2-carboxamide; and
30 N-[2-(3-(2-propylamino)-3-oxo-2,2-difluoro-1-oxopropyl)phenyl]2-methoxyphenylcarboxamide.

28. The method of Claim 19 wherein the subject is infected with a herpesvirus selected from herpes simplex virus type-1 (HSV-1), herpes
35 simplex virus type-2 (HSV-2), cytomegalovirus (CMV), varicella-zoster virus (VZV), Epstein-Barr virus, herpesvirus-6 (HHV-6), herpesvirus-7 (HHV-7), herpesvirus-8 (HHV-8), pseudorabies and rhinotracheitis.

29. A method of inhibiting a viral protease, said method comprising treating said subject with an effective amount of a compound of Claim 1.

5 30. Method of Claim 19 wherein the viral protease is a herpesvirus protease.

31. Method of Claim 30 wherein the viral protease is selected from a CMV protease, an HSV-1 protease and a HSV-2 protease.

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32. Method of Claim 31 wherein the viral protease is a CMV protease, encoded by U_L80.

33. A method of prophylactic treatment of herpes viral infection
15 in a subject, said method comprising treating said subject with an effective amount of a compound of Claim 1.

34. The method of Claim 33 wherein the herpesvirus is selected
from herpes simplex virus type-1 (HSV-1), herpes simplex virus type-2
20 (HSV-2), cytomegalovirus (CMV), varicella-zoster virus (VZV), Epstein-Barr virus, herpesvirus-6 (HHV-6), herpesvirus-7 (HHV-7), herpesvirus-8 (HHV-8), pseudorabies and rhinotracheitis.

25 **ELECTROPHILIC KETONES FOR THE TREATMENT OF
HERPESVIRUS INFECTIONS**

ABSTRACT

30 A class of compounds is described which can be used for the treatment of viral infections. Compounds of particular interest are defined by Formula II